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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Complete if Known

Application Number	09/834,792
Filing Date	April 13, 2001
First Named Inventor	Margolskee
Art Unit	1647
Examiner Name	Sharon L. Turner
Attorney Docket Number	34116/1051

U.S. PATENT DOCUMENTS

Examiner Initials ¹	Cite No. ¹	U.S. Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code ³ (if known)			
SJ	1	US-2004/0259160 A1	12/23/2004	Johnson et al.	
	2	US-4,376,110	03/08/1983	David et al.	
	3	US-4,873,191	10/10/1989	Wagner et al.	
	4	US-4,946,778	08/07/1990	Ladner et al.	
SJ	5	US-5,585,089	12/17/1996	Queen et al.	

FOREIGN PATENT DOCUMENTS

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		Country Code ³ Number ⁴ Kind Code ³ (if known)				
SJ	6	DE 199 53 167 A1	07/26/2001	Johannes-Gutenberg-Universität Mainz		X
	7	WO 00/40969	07/13/2000	Sippel et al.		X
	8	WO 01/32693 A2	05/10/2001	Johannes-Gutenberg-Universität Mainz		X
	9	WO 01/79448 A2	10/25/2001	Mount Sinai School of Medicine of New York University		
	10	WO 02/054069 A1	07/11/2002	The Regents of the University of California		
	11	WO 02/087306 A2	11/07/2002	Senomyx, Inc.		
	12	WO 02/10382 A2	02/07/2002	Wissenbach, Ulrich		
SJ	13	WO 2004/076632 A2	09/10/2004	The Queen's Medical Center		

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials ¹	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
SJ	14	Akabas et al., "A Bitter Substance Induces a Rise in Intercellular Calcium in a Subpopulation of Rat Taste Cells," <i>Science</i> 242:1047-1050 (1988)	
	15	Asano-Miyoshi et al., "Co-Expression of Calcium Signaling Components in Vertebrate Taste Bud Cells," <i>Neurosci. Lett.</i> 283:61-64 (2000)	
SJ	16	Ausubel et al., "Current Protocols in Molecular Biology," Vol. 2, Green Publishing Associates, Inc. and John Wiley and Sons, Inc., New York, pp.2.10.2-2.10.3 (1989)	

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Sharon L. Turner

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	17	Baxter et al., "A Novel Membrane Potential-Sensitive Fluorescent Dye Improves Cell-Based Assays for Ion Channels," <i>J. Biomol. Screen.</i> 7(1):79-85 (2002)	
	18	Behrendt et al., "Characterization of the Mouse Cold-Menthol Receptor TRPM8 and Vanilloid Receptor Type-1 VR1 Using a Fluorometric Imaging Plate Reader (FLIPR) Assay," <i>Brit. J. Pharmacol.</i> 141(4):737-745 (2004)	
	19	Bernhardt et al., "Changes in IP ₃ and Cytosolic Ca ²⁺ in Response to Sugars and Non-Sugar Sweeteners in Transduction of Sweet Taste in the Rat," <i>J. Physiol.</i> 490.2:325-336 (1996)	
	20	Bird et al., "Single-Chain Antigen-Binding Proteins," <i>Science</i> 242(4877):423-426 (1988)	
	21	Bobanovic et al., "Molecular Cloning and Immunolocalization of a Novel Vertebrate <i>trp</i> Homologue from <i>Xenopus</i> ," <i>Biochem. J.</i> 340:593-599 (1999)	
	22	Bronstein et al., "Chemiluminescent Reporter Gene Assays: Sensitive Detection of the GUS and SEAP Gene Products," <i>Biotechniques</i> 17(1):172-177 (1994)	
	23	Chomczynski & Sacchi, "Single-Step Method of RNA Isolation by Acid Guanidinium Thiocyanate-Phenol-Chloroform Extraction," <i>Anal. Biochem.</i> 162:156-159 (1987)	
	24	Cole et al., "The EBV-Hybridoma Technique and Its Application to Human Lung Cancer," in <i>Monoclonal Antibodies and Cancer Therapy</i> , Alan R. Liss, Inc., pp.77-96 (1985)	
	25	Cote et al., "Generation of Human Monoclonal Antibodies Reactive with Cellular Antigens," <i>Proc. Natl. Acad. Sci. USA</i> 80:2026-2030 (1983)	
	26	Creighton, T.E., "Proteins: Structures and Molecular Principles," W.H. Freeman & Co., New York (1983) (Table of Contents Only)	
	27	Enklaar et al., " <i>Mir1</i> , a Novel Biallelically Expressed Gene in the Center of the Mouse Distal Chromosome 7 Imprinting Cluster, is a Member of the <i>Trp</i> Gene Family," <i>Genomics</i> 67:179-187 (2000)	
	28	Falconer et al., "High-Throughput Screening for Ion Channel Modulators," <i>J. Biomol. Screen.</i> 7(5):460-465 (2002)	
	29	Filmore, D., "Cell-Based Screening Assays and Structural Studies are Fueling G-Protein Coupled Receptors as One of the Most Popular Classes of Investigational Drug Targets," <i>Modern Drug Discovery</i> pp.24-26, 28 (2004)	

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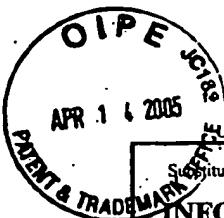
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SS	30	Fleig et al., "Emerging Roles of TRPM Channels," in "Mammalian TRP Channels as Molecular Targets," <i>Novartis Foundation Symposium 258</i> , John Wiley & Sons, Ltd. pp.248-266 (2004)	
	31	GenBank Accession No. AC003693 (September 30, 1998)	
	32	GenBank Accession No. AF177473 (January 20, 2000)	
	33	Gilbertson et al., "The Molecular Physiology of Taste Transduction," <i>Curr. Opin. Neurobiol.</i> 10:519-527 (2000)	
	34	Gill et al., "Flux Assays in High Throughput Screening of Ion Channels in Drug Discovery," <i>Assay and Drug Dev. Tech.</i> 1(5):709-717 (2003)	
	35	Gordon, J.W., "Transgenic Animals," <i>Intl. Rev. Cytol.</i> 115:171-229 (1989)	
	36	Herness, M.S., "Cellular Mechanisms of Taste Transduction," <i>Ann. Rev. Physiol.</i> 61:873-900 (1999)	
	37	Hofmann et al., "TRPM5 is a Voltage-Modulated and Ca ²⁺ -Activated Monovalent Selective Cation Channel," <i>Current Biol.</i> 13:1153-1158 (2003)	
	38	Hoon et al., "Putative Mammalian Taste Receptors: A Class of Taste-Specific GPCRs with Distinct Topographic Selectivity," <i>Cell</i> 96:541-551 (1999)	
	39	Houghten et al., "Generation and Use of Synthetic Peptide Combinatorial Libraries for Basic Research and Drug Discovery," <i>Nature</i> 354:84-86 (1991)	
	40	Huang et al., "Gy13 Colocalizes with Gustducin in Taste Receptor Cells and Mediates IP ₃ Responses to Bitter Denatonium," <i>Nat. Neurosci.</i> 2(12):1055-1062 (1999)	
SS	41	Huston et al., "Protein Engineering of Antibody Binding Sites: Recovery of Specific Activity in an Anti-Digoxin Single-Chain Fv Analogue Produced in <i>Escherichia coli</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 85:5879-5883 (1988)	

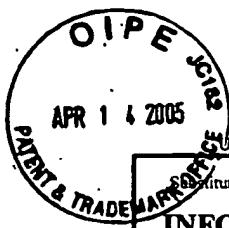
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Attorney Docket Number	34116/1051

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	42	Kinnamon & Margolskee, "Mechanisms of Taste Transduction," <i>Curr. Opin. Neurobiol.</i> 6(4):506-513 (1996)	
	43	Köhler & Milstein, "Continuous Cultures of Fused Cells Secreting Antibody of Predefined Specificity," <i>Nature</i> 256:495-497 (1975)	
	44	Komuro & Rakic, "In Vitro Analysis of Signal Mechanisms Involved in Neuronal Migration," in L.W. Haynes ed., <i>The Neuron in Tissue Culture</i> , New York: John Wiley & Sons, pp.57-69 (1999)	
	45	Kozbor & Roder, "The Production of Monoclonal Antibodies from Human Lymphocytes," <i>Immunology Today</i> 4(3):72-79 (1983)	
	46	Lakso et al., "Targeted Oncogene Activation by Site-Specific Recombination in Transgenic Mice," <i>Proc. Natl. Acad. Sci. USA</i> 89:6232-6236 (1992)	
	47	Lam et al., "A New Type of Synthetic Peptide Library for Identifying Ligand-Binding Activity," <i>Nature</i> 354:82-84 (1991)	
	48	Lavitrano et al., "Sperm Cells as Vectors for Introducing Foreign DNA into Eggs: Genetic Transformation of Mice," <i>Cell</i> 57:717-723 (1989)	
	49	Lindemann, B., "Receptors and Transduction in Taste," <i>Nature</i> 413:219-225 (2001)	
	50	Lindemann, B., "Taste Reception," <i>Physiological Reviews</i> 76(3):719-766 (1996)	
	51	Liu & Liman, "Intracellular Ca ²⁺ and the Phospholipid PIP ₂ Regulate the Taste Transduction Ion Channel TRPM5," <i>PNAS</i> 100(25):15160-15165 (2003)	
	52	Lo, C.W., "Transformation by Iontophoretic Microinjection of DNA: Multiple Integrations Without Tandem Insertions," <i>Mol. Cell Biol.</i> 3(10):1803-1814 (1983)	
	53	McLaughlin et al., "Gustducin is a Taste-Cell-Specific G Protein Closely Related to the Transducins," <i>Nature</i> 357:563-569 (1992)	
	54	Ming et al., "Blocking Taste Receptor Activation of Gustducin Inhibits Gustatory Responses to Bitter Compounds," <i>Proc. Natl. Acad. Sci. USA</i> 96:9903-9908 (1999)	

Examiner Signature

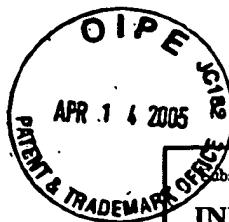
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	55	Ming et al., "Characterization and Solubilization of Bitter-Responsive Receptors That Couple to Gustducin," <i>Proc. Natl. Acad. Sci USA</i> , 95:8933-8938 (1998)	
	56	Montell, C., "New Light on TRP and TRPL," <i>Mol. Pharmacol.</i> 52:755-763 (1997)	
	57	Morrison et al., "Chimeric Human Antibody Molecules: Mouse Antigen-Binding Domains with Human Constant Region Domains," <i>Proc. Natl. Acad. Sci. USA</i> 81:6851-6855 (1984)	
	58	Neuberger et al., "Recombinant Antibodies Possessing Novel Effector Functions," <i>Nature</i> 312:604-608 (1984)	
	59	Ninomiya et al., "Lack of Gurmarin Sensitivity of Sweet Taste Receptors Innervated by the Glossopharyngeal Nerve in C57BL Mice," <i>Am. J. Physiol.</i> 272(3 Pt 2):R1002-1006 (1997)	
	60	Perez et al., "A Transient Receptor Potential Channel Expressed in Taste Receptor Cells," <i>Nature Neurosci.</i> 5(11):1169-1176 (2002)	
	61	Prawitt et al., "Identification and Characterization of <i>MTR1</i> , A Novel Gene With Homology to Melastatin (<i>MLSN1</i>) and the <i>trp</i> Gene Family Located in the BWS-WT2 Critical Region on Chromosome 11p15.5 and Showing Allele-Specific Expression," <i>Human Molecular Genetics</i> , 9(2):203-216 (2000)	
	62	Ruiz-Avila et al., "Coupling of Bitter Receptor to Phosphodiesterase Through Transducin in Taste Receptor Cells," <i>Nature</i> 376:80-85 (1995)	
	63	Sambrook et al., "Molecular Cloning," 2 nd Ed. Cold Spring Harbor Laboratory Press (1989) (Table of Contents only)	
	64	Songyang et al., "SH2 Domains Recognize Specific Phosphopeptide Sequences," <i>Cell</i> 72:767-788 (1993)	
	65	Takeda et al., "Construction of Chimaeric Processed Immunoglobulin Genes Containing Mouse Variable and Human Constant Region Sequences," <i>Nature</i> 314:452-454 (1985)	
	66	Thompson et al., "Germ Line Transmission and Expression of a Corrected HPRT Gene Produced by Gene Targeting in Embryonic Stem Cells," <i>Cell</i> 56:313-321 (1989)	

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SJ	68	Ward et al., "Binding Activities of a Repertoire of Single Immunoglobulin Variable Domains Secreted from <i>Escherichia coli</i> ," <i>Nature</i> 341:544-546 (1989)	
SJ	69	Wolff et al., "Comparative Study of Membrane Potential-Sensitive Fluorescent Probes and Their Use in Ion Channel Screening Assays," <i>J. Biomol. Screening</i> 8(5):533-543 (2003)	
SJ	70	Xu et al., "Ion-Channel Assay Technologies: <i>quo vadis?</i> ," <i>Drug Discov. Today</i> 6(24):1278-1287 (2001)	

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